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PATENT & TRADEMARK OFFICE

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W. Lowe
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S/N 09/125,953

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	FOSTAD ET AL.	Examiner:	B. SISSON
Serial No.:	09/125,953	Group Art Unit:	1655
Filed:	December 10, 1998	Docket No.:	7885.56USWO
Title:	IMMUNO-MAGNETIC CELL SEPARATION USED IN IDENTIFICAITON OF GENES ASSOCIATED WITH SITE-PREFERENCED CANCER METHASTASIS FORMATION		

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited in the United States Postal Service, as first class mail, with sufficient postage, in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on March 6, 2000.

By: _____
Name: John J. Gresens

RESPONSE

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Responsive to the Office Action dated December 6, 1999, Applicants submit the following remarks.

REMARKS

Applicants thank the Examiner for the care and time taken in consideration of the above–referenced patent application and claims.

112 Rejections

The Examiner rejected claims 10 and 11 under 35 U.S.C. 112, first paragraph. Applicants respectfully traverse this rejection.

Claim 10

The Examiner stated that the method of claim 10 is drawn to the use of previously unknown genes in gene therapy and that an undue burden would be placed on the public or skilled artisan to identify these unknown genes and develop the required methods of

their use in gene therapy. The Examiner further stated that when there is no disclosure of any specific starting material or of any of the conditions under which process can be carried out, undue experimentation is required, and it is the specification, not the knowledge of one of skill in the art, that must supply the novel aspects of invention in order to constitute an adequate written description.

The method of claim 10 is directed to genes which are previously unknown, but identified by using the present method. The method of the claimed invention provides a means for one of skill in the art to identify previously unknown genes and the specification provides enablement for such a method. The claimed method is designed to identify genes which are differentially expressed in different tissues. This is exemplified, for example, in the enclosed journal article, Ree et al. Cancer Res 59:4675–4680 (1999), which demonstrates identification of a new gene product (candidate of metastatis–1) by the method according to the presently claimed invention.

When inventors identify differentially expressed genes; e.g. in a metastatic cell growing in the lung, it may mean that such growth is facilitated by expression of one or several of the specifically identified genes. The next step would naturally be to attack such a gene by, for example, gene therapy. Such methods are known to the artisans in the field. One of many examples is provided in the second enclosed journal article, Maelandsmo et al. Cancer Res 56:5490–5498 (1996), wherein a hammerhead ribozyme is used to knock out the specific gene sequence and a resulting reduction of the expression of the metastatic gene and a consecutive reduction of metatstatic capability was obtained. This demonstrates the use of gene therapy with a previously unknown gene sequence and demonstrates that it is clearly within the ability of one of skill in the art to perform gene therapy experiments.

Thus, given the specification of the present application, it is well within the abilities of one skilled in the art to identify a gene sequence which can then be attacked by gene therapeutic means.

Claim 11

The Examiner stated that Claim 11 is drawn to obtaining specific genes and their expression products and that the resultant expression products are unlimited. The Examiner further stated that the specification does not set forth a repeatable procedure whereby one of skill in the art would be able to produce the expression product for any

gene isolated from any target cell. The Examiner further stated that what these gene products are and how their activity and use is to be ascertained is left to the skilled artisan to determine, and that such reliance upon the skilled artisan to provide the novel aspects of the invention is improper.

The presently claimed method comprises a combination of immuno–magnetic techniques of specific target cells and gene cloning procedures for identifying genes with site–specific or site–preferred expression, and the use of such methods to obtain specific gene sequences in target cells. Once such specific gene sequences are identified according to the method of the invention, it is well within the abilities of one of skill in the art to obtain the specific gene sequences and their expression products. Examples of methods of obtaining gene sequences and their expression products are shown, for example, in Maaelandsmo et al., Cancer Res. 56:5490–5498 (1996), and reference 4 and 35 in this article, and in Ree et al., Cancer Res. 59:4675–4680 (1999).

Thus, given the specification of the present application, it is well within the abilities of one skilled in the art to identify a gene sequence and obtain the gene sequence and its expression products. Withdrawal of the rejection is respectfully requested.

Anticipation Rejection

The Examiner rejected claims 1–9 under 35 U.S.C. 102(b) as allegedly being anticipated by Høifødt et al. (WO 95/24648). Applicants respectfully traverse this rejection.

The claimed method comprises a combination of immuno–magnetic techniques of specific target cells (WO95/24648, Fodstad et al.) and gene cloning procedures for identifying genes with site–specific or site–preferred expression, and the use of such methods to obtain specific gene sequences in target cells. Thus the claimed method is directed to identify unknown genes which are expressed differentially in cells, such as tumor cells, in different tissues or organs.

The Examiner stated that Høifødt et al. disclose a method for identifying genes with site–specific or site preferred expression in specific target cells wherein said target cells are initially detected and isolated by repeated immunomagnetic procedures; wherein the target cells can be malignant cells, including those found in bone marrow, blood, other bodily fluids, tumors, etc; wherein the target cells can be cultured and subjected to further biochemical analysis, including conducting PCR on cDNA derived from RNA.

The reference does not, however, mention nor suggest gene cloning to study differences in mRNA expression levels by comparison. Neither was this in the minds of the inventors because at that time, and even now regarding some persons with skill in the art, the general knowledge taught that the reason that certain metastatic tumor cells preferred certain tissues most probably was caused by selection in the primary tumor cells with a particular "metastatic capacity", which when distributed in the body would grow in any tissue providing a fertile soil. Up– and down–regulation of specific genes in the tumor cells, caused by interaction with nornmal cells, different from one tissue/organ to another, was not known or contemplated. When the presently claimed method was tried for the first time it represented guess work on the part of the inventors, and when they obtained the results described in the examples of the present specification they were surprised, and so were doubting colleagues. Recent studies have now revealed that the gene LV1 in Example 2 is a previously unknown gene which does not belong to any known gene family.

Applicants respectfully assert that the claimed method is not obvious over Høifødt et al. and respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants respectfully assert that the instant claims are in a condition for allowance.

If the Examiner has any questions regarding the foregoing, it is respectfully requested that he call the undersigned.

Respectfully submitted,

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March 6, 2000
Date

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